
*THE SCIENCE
OF FERMENTS,
FERMENTATION,
THE MICROBIOTA,
& THE HEALTH
OF YOGURT*

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A. General overview

Danone's story starts with the vision of two extraordinary men: the 1st one is a renowned and passionate scientist, the other, the founder of Danone, driven by the desire to supply a delicious food with health benefits.

Yogurt is a magic product. Known and renowned for its qualities based on common popular wisdom, it has become part of nutrition habits that date back to several thousands of years. This magical status comes from its lactic ferments, probiotics and essential nutritional ingredients that are part of its make-up and allow for proper storage. While it is a fully natural product, it is also a highly scientific food that can be consumed every day and that can even be suitable for lactose mal digesters. It contains a cocktail of essential nutrients of which proteins, vitamins and numerous minerals such as calcium and potassium.

Once tasted and then consumed, its main site of action is located at the level of the gut flora or microbiota. This part of the human body fascinated Elias Metchnikoff for whom we are celebrating the 100th anniversary of his passing away. The microbiota is under the spotlights of numerous scientists who see in it an extraordinary potential through its numerous and varied interactions with body function.

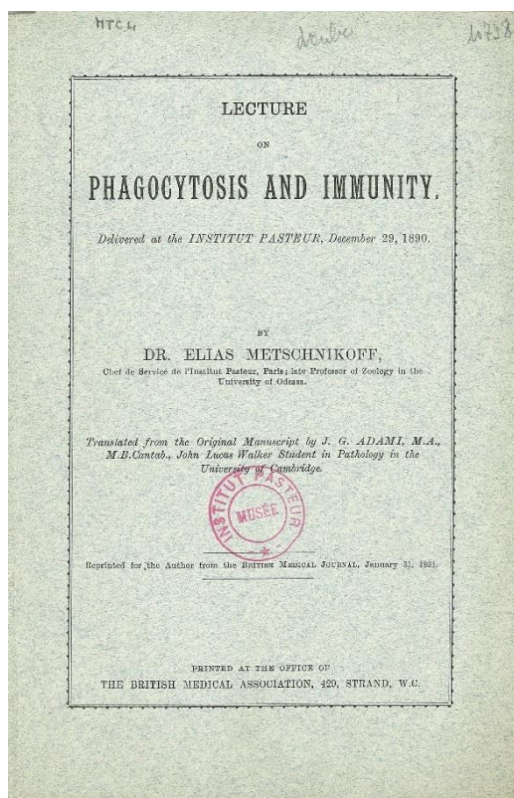
Indeed, thanks to recent scientific and technological advances in the area of the microbiota, new doors are being opened for solutions based on nutrition that may contribute to our health and well-being. It is of utmost importance to note that beyond the impact of certain ferments and other yogurt ingredients on health, there are thousands of ways of using ferments to offer flavors and textures that are adapted to the desires of each and every one. Thanks to its strain collection, Danone has access to an infinite number of possibilities that can be explored to respond to consumer needs around the world. Science is continuing to progress at Danone and participate in the development of new offers taking into consideration nutrition habits and desires that are both for health and for pleasure.

B. Elias Metchnikoff, 1st observer of the health benefits of microorganisms

2016 marks the 100th year since the passing away of Elias Metchnikoff, the father of gerontology, phagocytosis and immunology. He was among the first scientists to look into the role of the gut microbiota on longevity. Born in the Ukraine, this brilliant student of physiology and science studied in Russia, Germany and Italy before being invited by Pasteur to conduct research in his newly opened institute. Metchnikoff not only accepted Pasteur's offer but ended up staying the last 28 years of his life in Paris where he was awarded, in 1908, with a Nobel Prize for his work on immunity.

The man who discovered phagocytosis

Metchnikoff was a relentless scientist, fascinated by the observations he was able to make.



He was also determined to make sense of what he was observing. One of his discoveries concerned the capacity of certain cells to engulf targets such as microbes or other pathogens, destroy them and prevent them from causing harm to the body. This process, defined as “phagocytosis” is at the heart of our immune system and explains why Elias Metchnikoff is considered to be one of the fathers of immunity.

This particular discovery was what allowed Metchnikoff to become co-laureate with Paul Ehrlich of the Nobel Prize of physiology or medicine. Paul Ehrlich also focused on how the immune system protects the body from attacks by microorganisms.

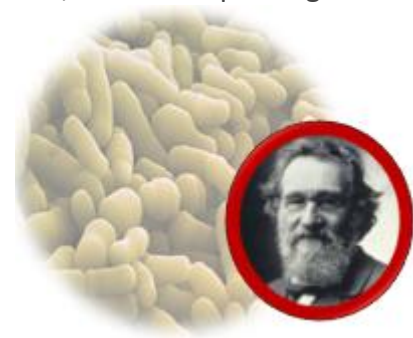
The interest developed in the role of microorganisms in our gut came from observations

made on how people living in the Balkans who regularly consumed fermented products had a tendency of aging better and living longer. Ferments are indeed special microorganisms, in the form of molds, yeast or bacteria, which have the ability to modify food substances. These microorganisms also interact with the bacteria that are already present in our gut.

Very first observations of the potential health benefits yogurt's ferments

With regard to what was going on in the gut, Elias Metchnikoff was the first person to have noticed the benefits of sour milk and lactic bacteria, especially *Lactobacillus bulgaricus*. Discovered in 1905 in Geneva by Stamen Grigorov within Leon Massol's laboratory, this ferment is still being used for the production of yogurt and fermented milks in association with *Streptococcus thermophilus*. Thanks to his observations of how lactic bacteria helped to prevent harmful putrefication processes that take place in the gut, Elias Metchnikoff opened the door to the importance of the role of the microbiota on human longevity and health. He has left an important scientific legacy, through his strong belief in the incredible power of ferments to prevent disease and offer greater well-being. This was the first time in history that scientists started to talk about the benefits on health of lactic ferments present in fermented milk products.

Metchnikoff's theory was that by compensating for the potentially harmful effects of toxins produced by bacteria in the gut, by these good lactic ferments, one could prolong life. This theory was supported by the fact that, among the people living in the Balkans, those whose diets contained high amounts of fermented dairy products, actually lived longer. This area of the Western world was known for its higher number of centenarians at a time when it was extremely rare for any human being to reach that age. Elias Metchnikoff himself adopted this type of a diet and claimed to feel better. It is this very science that is at the origin of the booming areas of research around the impact of the microbiome on health.



C. Isaac Carasso – founder of Danone

Born in 1874 in the Balkans, a relatively harsh and mountainous region of Southeastern Europe, Isaac Carasso was quite familiar with the overall health benefits of fermented dairy products and in particular their benefits on digestive disorders. As war started to break out within this region ruled by the Ottoman Empire, Carasso decided to move his family to Spain, a country his ancestors fled under the 15th Century Spanish Inquisition. Once in Barcelona, he noticed that many young children were suffering from digestive problems including severe diarrhea. Remembering the traditions of his native Balkans, he immediately thought about making yogurt available to prevent potentially serious consequences of such disorders.

Sales of yogurt in pharmacies in Spain to prevent childhood digestive disorders

Inspired by the work of Elias Metchnikoff, Isaac Carasso contacted the Pasteur Institute to acquire ferments that will enable the production of the first ever industrialized yogurts in 1919. These cultures were isolated by the Pasteur Institute. Named after Isaac's son Daniel, whose diminutive is "Danone" in Catalan, these yogurts were sold, through pharmacies before being offered to stores able to sell fresh refrigerated dairy products. This is how Danone's first product aimed at "bringing health through food to as many people as possible" was brought to market. It is therefore, thanks to Elie Metchnikoff's science and to Isaac Carasso's vision, that Danone developed early on an interest in ferments, fermentation and the microbiota.



D. Ferments and fermentation

Ferments are living microorganisms that transform food into fermented products. Among the different microorganisms that are involved in food transformation are molds, yeast and bacteria. Examples of popular fermented products include wine, bread, Sauerkraut, kefir, Korean Kimchi and of course yogurt. These recipes have all undergone a fermentation process that not only affects their taste and texture but also contributes to better storage.

A large variety of traditions of fermented dairy products around the world

Fermentation always takes place within a matrix. It is a metabolic process by which complex carbohydrates or sugars are broken down into acids, gases or alcohol. The three main types of fermentation include: lactic fermentation leading to yogurt, kimshi, sauerkraut and other foods, alcoholic fermentation leading to wine, beer and other alcoholic beverages, and acetic fermentation mostly known to produce vinegar. The process can take place externally in foods or internally within our own gut which represents the most important fermentation site in human beings. This breakdown produces energy and accounts for the synthesis of vitamin K and certain B vitamins.

EXAMPLES OF TRADITIONAL FERMENTED DAIRY PRODUCTS AROUND THE WORLD:



The transforming powers of ferments have been the subject of myths for thousands of years. Today, they have become the subject of scientific scrutiny as Danone continues to build its expertise in strain analyses, selection and combination and in the fermentation process.

Let's remember that lactic fermentation is a natural process involving the production of lactic acid. It brings 3 major benefits including:

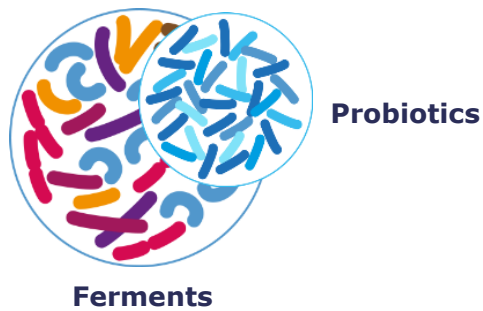
1. Natural food preservation properties: by limiting the growth of bad bacteria responsible for the development of putrefaction and molds, allowing yogurt thereby to be preserved 100% naturally. This is how fermentation became the first natural preservation method for certain foods.
2. Organoleptic properties or those that influence the fermented product's taste, smell and texture, and specific properties that facilitate lactose digestion. Fermentation is associated with the formation of an amazing fragile lacy construction during which blocks of protein gradually come together. This incredible transformation produces a new texture and new aromas. In fact, there are as many different yogurt flavors and textures as there are varieties of ferments. So there is a wealth of opportunities to produce delicious yogurts out there.
3. Facilitated lactose digestion: ferments contain indeed enzymes that are able to predigest lactose, which is of particular interest to lactose mal digesters.

Danone: a large collection of microorganisms to create new fermented products

Danone Nutricia Research has strong expertise in ferments. This expertise spans the entire value chain of the fermentation process, from the selection of specific bacterial strains to the development of new tasty and healthy fermented milks. The unique in-house collection of close to 4,000 microorganisms, or ferments, offers Danone Nutricia Research countless opportunities to innovate and develop future generations of yogurt and other fermented products. These ferments can play a role in the taste, texture as well as the health benefits when they act as probiotics. The World Health Organization (WHO) has defined probiotics as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host".

Thus, Danone's large collection of bacterial strains allows it to propose many different types of tests, combining different strains to **introduce new products that are** better able to meet both the needs of populations with regards to their **health and well-being** as well as their

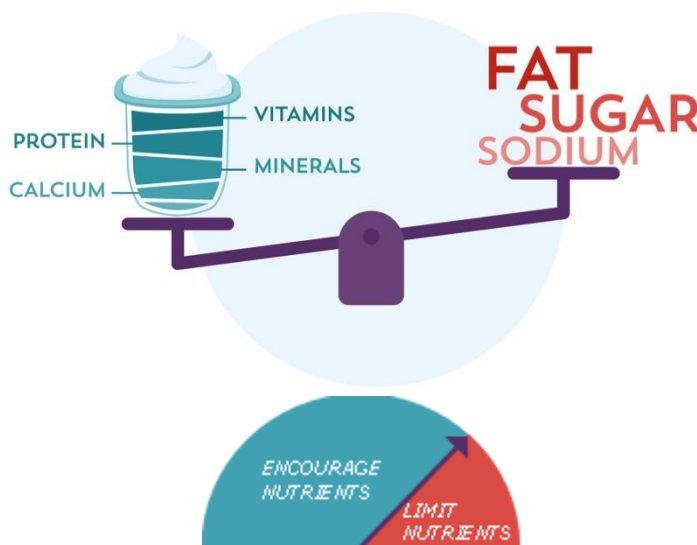
desire for **pleasurable eating experience**. It is important to note however, that not all probiotics possess the natural enzymatic properties that are required to launch a fermentation process. Thus, some of them are not ferments and all ferments are not probiotics.



E. The health of yogurt

Yogurt is a fermented dairy product and a nutritious food containing a host of vitamins, minerals, proteins and carbohydrates that are essential to health. Depending on the type of yogurt one chooses, it is possible to find fair to relatively large amounts of potassium, calcium, magnesium, phosphorus, thiamin, riboflavin, niacin, folate, fibers, Vitamins A, B, C and D and even some iron. Yogurt contributes to a multitude of essential daily nutrient requirements such as the contribution of up to **10-20% of the average daily guideline amounts of calcium per 100g serving.**

For people who have difficulties in digesting fresh milk products because they are lactose mal digesters, the good news is that yogurt is an option. It contains the bacterial enzymes that can digest lactose thereby eliminating all worries they may have about their own inability to break it down.



While the benefits of regular dairy product intake on bone health are quite known, additional data on the role of regular yogurt is now being produced. Just as Elias Metchnikoff noted in an empirical manner, these new data are confirming that regular consumers of yogurt are less prone to heart diseases and other health issues. Recent studies are even showing that they generally have healthier lifestyles and tend to live longer.

These health benefits last over time. Other health parameters observed with regular yogurt consumption include a better weight profile and reduced weight gain during life as well as reductions in high blood pressure and risk of type 2 diabetes. Still other ongoing studies are currently exploring how yogurt affects these health parameters and indicate a potential effect of lactic bacteria or the food matrix (the milk) on the nutritional components of yogurt.

Because yogurt has so many assets, scientists are now trying to better understand what role is played by its different nutritional components and in particular the lactic bacteria or ferments contained in the food matrix itself. Even though there is so much more to learn about the benefits of yogurt, food pyramids and dietary guidelines in various parts of the world are already advocating yogurt as a food for daily consumption at all ages in healthy diets.

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F. The science of the microbiota

Elias Metchnikoff was among the first scientists to talk about the gut microbiota or gut flora which he defined as a complex intestinal arrangement that forms a breeding place for poisonous microbes. In an article published in January 1908, Metchnikoff stated that it is possible to combat the putrefaction that takes place in this area, notably by means of diet or hygiene. Doing so will increase one's chances to attain a healthy and vigorous old age.

Gut health & microbiota: a booming area of research

Today, gut related scientific research is booming worldwide. Projects are being funded by both industries and governments who see great promise for providing people with new ways to adopt healthier lifestyles and moreover, prevent certain diseases. Two major projects, launched in 2008, account for this growing interest in gut health: the European MetaHIT project and the US Human Microbiome Project (HMP).

Launched in 2008, MetaHIT was the largest European project aimed at sequencing the genome of the microbiota. Danone, who has been a strong believer in this field of science, was the only food company to invest in this project.

During that same year, the NIH (National Institutes of Health) established a Common Fund for a Human Microbiome Project (HMP) to gather necessary resources for a full characterization of the human microbiome and analysis of its role in human health and disease.

Since then, thousands of papers have been published on this core topic in various peer reviewed publications. The number of articles published each year has been growing consistently over the last 10 years. It is expected that this trend will continue.

One of the main reasons why this science is booming is linked to the development of specific gene sequencing tools and artificial models that did not exist 10 years ago. Because there are many different types of bacteria that make up the microbiome, it is important to be able to distinguish them as precisely as possible, before making any general conclusions.

Metabolic and brain function: new perspectives for gut health

A strong testimony to the growing interest in the microbiota lies within the Harvard Medical School Division of Nutrition symposia on Gut Health, Microbiota & Probiotics throughout the Lifespan.

Danone Nutricia Research one of the leading sponsors continues to support research in the emerging field of the microbiome and its interactions with body functions.

This event gathered several hundred specialists in the various fields of science and medicine. Discussions centered on two of the world's most important public health issues: metabolic and brain function. On this occasion, leading researchers from around the world were able to exchange on emerging science around the role of the gut microbiota in obesity, diabetes, cardiovascular and gastrointestinal diseases as well as certain chronic brain disorders.

Because all the foods we eat come into contact with the microorganisms of our gut, this exploding area of science will certainly offer new insights into the types of diets that may help to program, protect or pamper the health of our gut.



You will find further information on this unique event on the following website:
<http://harvardprobioticssymposium.org/>

G. Daniel Carasso Research Center

While young Daniel Carasso was growing up, he knew that he would be taking over his father's yogurt business. To reinforce his understanding of the science of ferments, he pursued an internship within the Pasteur Institute. Thanks to this experience, it became quickly obvious to Daniel that the family business needed to develop its own research capabilities in addition to maintaining strong ties with external research centers including, of course, the Pasteur Institute.

Opened finally in 2002, the Danone's Daniel Carasso R&D center is Danone's first research center dedicated to research on fresh dairy products and waters. This center was the first within the Paris-Saclay innovation cluster which today has become home to prestigious academic institutions and research laboratories. The research activities around fresh dairy products are state of the art and extremely broad in scope. They aim to find ways to launch innovations to satisfy the needs and desires of consumers. The dairy R&D consists of roughly 660 people located in 40 different countries for greater proximity with local needs. This team has been able to generate 140 scientific papers over the last 5 years, in peer-reviewed publications.

Today, this center is involved in projects that test how various ferments from Danone's unique strain collection interact with each other within the food matrix, as well as their influence on taste, texture and health. Danone's impressive strain collection has been built over a period of 90 years and currently contains close to 4 000 microorganisms. The center houses the

largest
full-
fledged
dairy
pilot
plant,
among
a total
of 18
Danone
pilot
sites.
The new



products can then be tested in the center's sensory lab where consumers are invited to share their reactions towards new product candidates. The collection of consumer insights follows very strict protocols.

Thus, even the evaluation of the organoleptic properties of Danone's fresh dairy products is done in a scientific manner.

Not alone, but with partners and stakeholders

Danone does not believe that it should explore the magic of ferments for dairy products alone. Hence major partnerships have been developed over the years with the world's most prestigious scientific institutions including Pasteur but also Harvard, INRA, University of Utrecht in Holland and Tufts University in the US. Danone Nutricia Research is currently pursuing partnerships for projects that concern its dairy division with 40 different organizations.

These partnerships span several different projects and aim to advance the technologies needed to analyze the microbiota and the research on the role of ferments on health.

H. About Danone

Dedicated to bringing health through food to as many people as possible, Danone is a leading global food company built on four business lines: Fresh Dairy Products, Early Life Nutrition, Waters and Medical Nutrition. Through its mission and dual commitment to business success and social progress, the company aims to build a healthier future, thanks to better health, better lives and a better world, for all its stakeholders—its 100,000 employees, consumers, customers, suppliers, shareholders and all the communities with which it engages.

Present in over 130 markets, Danone generated sales of €22.4 billion in 2015, with more than half in emerging countries. Danone's brand portfolio includes both international brands (Activia, Actimel, Danette, Danonino, Danio, evian, Volvic, Nutrilon/Aptamil, Nutricia) and local brands (Oikos, Prostokvashino, Aqua, Bonafont, Mizone, Blédina, Cow & Gate).

Listed on Euronext Paris and on the OTCQX market via an ADR (American Depositary Receipt) program, Danone is a component stock of leading social responsibility indexes including the Dow Jones Sustainability Indexes, Vigeo, the Ethibel Sustainability Index and the FTSE4Good Index.

For more information please visit: <http://www.danone.com/en/#>

I. About Danone Nutricia Research

R&D is at the very heart of Danone's mission: "bringing health through food to as many people as possible". Danone Nutricia Research combines the research and innovation of Danone to build bridges between science and nutrition, to create an enjoyable sensory experience, to adapt the products to different cultural and eating habits all over the world, and to improve the nutritional quality and environmental sustainability of our food.

This vision is supported by 4 fields of innovation:

- Reliability: committing to nutritional quality and managing natural resources sustainably,
- Progress: building bridges between science and nutrition to contribute to people's health,
- Cultures: linking food styles to local needs and create a unique consumer experience, meeting people's expectations, whatever their origin and culture,
- Well-being: supporting daily health and well-being for all, through guiding and building points of reference.

Our teams of 1,500 researchers and developers are split into two global research centers (Danone Research in France, Nutricia Research in the Netherlands), a few specialized centers (Nutricia Research in Singapore, Danone Research Packaging in France and Danone Research Fresh Dairy Technological Expertise in Spain) and into R&D branches. They collaborate through more than 200 partnerships with the most recognized international scientific communities in their field

J. Media Contacts

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